Tissue Engineering

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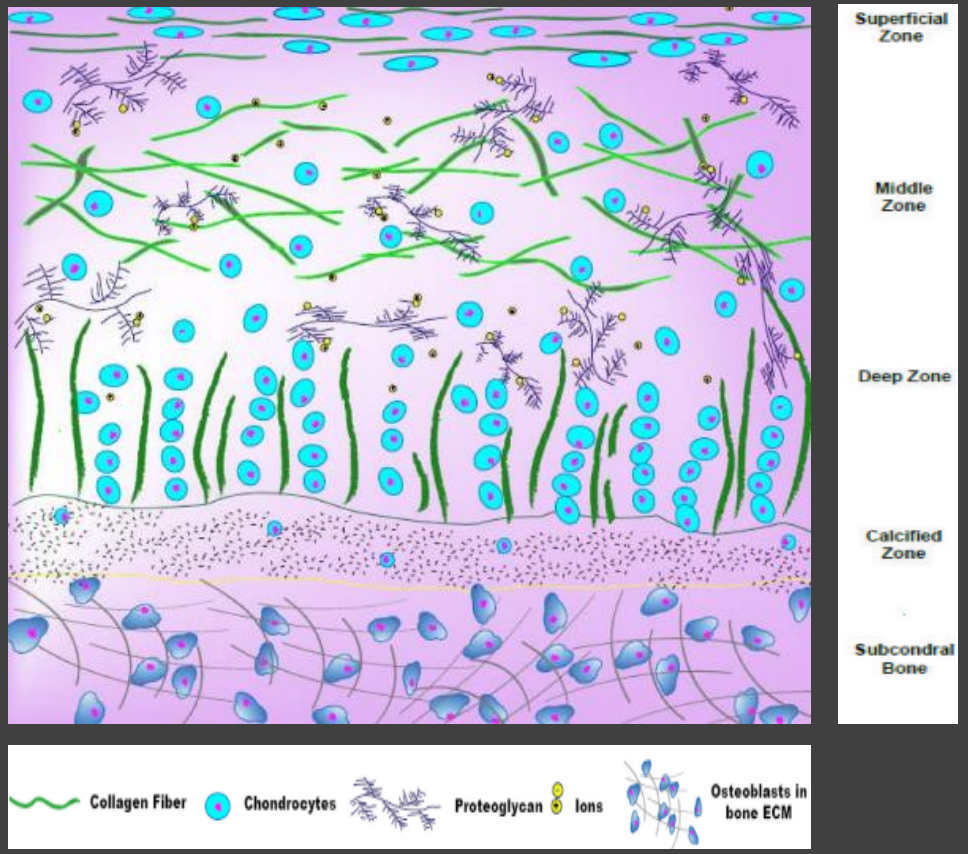
Articular Cartilage Structure

Four zones:

- Superficial
- Intermediate(middle)
- Deep
- Calcified cartilage zones

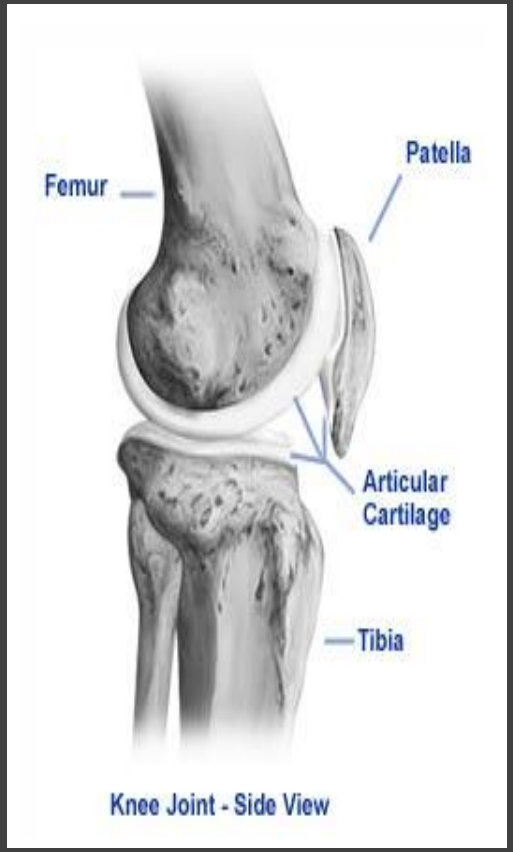


Composition

- Articular Cartilage is mainly composed of hyaline Cartilage, which is found on articulating surfaces of bones in diarthroidal joints. It is distinguished by high content of collagen type II and rich proteoglycan matrix, synthesized by chondrocytes.

Mechanical Function

- This surface acts as a shock absorber for the loads experienced due to body movement. This tissue provides lubrication and pain free motion with wear resistance over the course of an individuals lifetime.



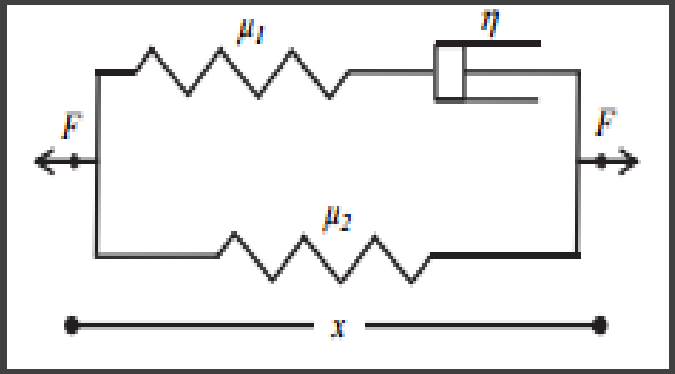
Analytic Composition of Articular Cartilage

Articular Cartilage		% wet weight[19,20]	% dry weight[21]	Functions
Solid Phase (ECM)	Collagen	Type II collagen is 15–20% All other collagens are < 2%	50–75%	Contributes to tensile properties and macromolecule entrapment[19,11]
	Proteoglycan	10%	20–30%	Contributes to compressive and flow-dependent viscoelastic properties[283]
	Other glycoprotein, fibronectin etc.	Small amount	Small amount	Contributes to cell-ECM interaction and the stability of ECM
Solid Phase (Cells)	Chondrocytes	< 5–10% of total tissue volume		Modify ECM and maintain suitable tissue size
Fluid Phase	Interstitial water and electrolytes	60–80%	—	Exchanges nutrients with synovial fluid, lubricates the joint, and contributes to compressive resistance and deformation[19]

Cartilage Injuries

Degradation of Cartilage can arise from:

- Trauma
- Degenerative joint Diseases
- Continual mechanical loading

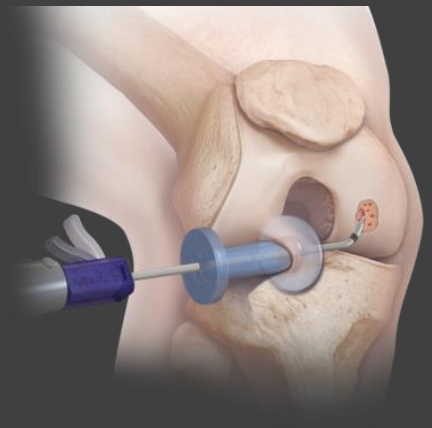


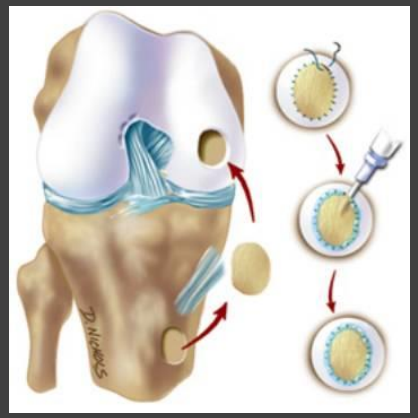
Types of cartilage injury:

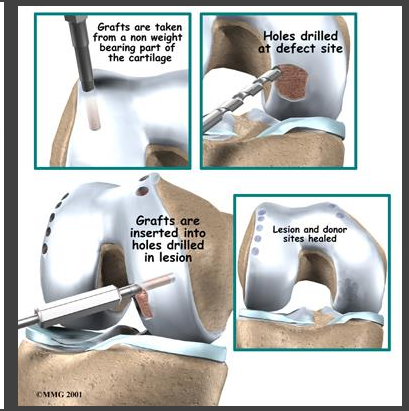
- Partial thickness defects
- Full thickness defects
- Superficial matrix disruption

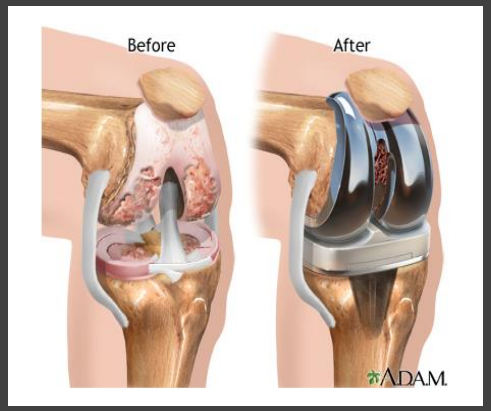
Cartilage Treatment

- Debridement and Lavage
- Microfracture
- Autologous Chondrocytes implantation
- Autografts and Allografts
- Total and Partial joint replacements





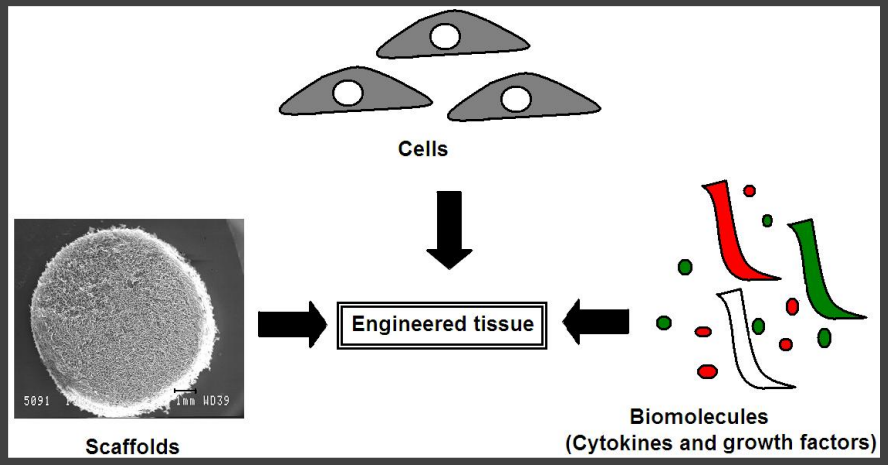




Tissue Engineering for articular cartilage repair

It uses principles and methods in engineering, material science, biology, and chemistry to develop biological substitutes that restore, maintain, or improve functionality of damaged tissues and organs.

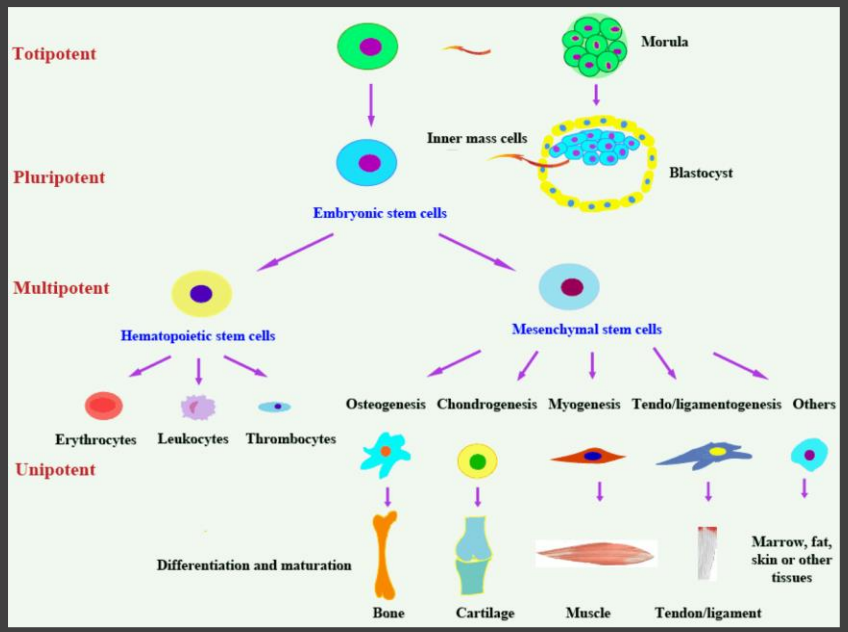
In the following sections, cells, scaffolds, bioactive factors, and mechanical stimuli for articular cartilage tissue engineering will be discussed.



Cells for Cartilage Defect Repair

- Chondrocytes
- Mesenchymal Stem Cells
- Embryonic Stem Cells

Type of stem cell	What it can be	Examples
Totipotent cells	Each cell can develop into a new individual	Cells of embryo of 1-3 days
Pluripotent cells	Each cell can form any cell type (over 200)	Cells of blastocyst 5-14 days
Multipotent cells	Cells differentiate and can form a number of tissue types.	Fetal tissue, cord blood, adult cells



Mesenchymal Stem Cells

MSCs	Advantages	Disadvantages
Bone marrow stem cells	• High chondrogenic potential • Homogeneous population	• Low yield (approximate 1 in 1 × 105 cells in the marrow)
Adipose-derived stem cells	• Abundance of tissue • High yield	• Inhomogeneous cell population
Infrapatellar fat pad-derived stem cells	• High chondrogenic potential • Low donor site morbidity	• Limited source of tissue
Synovium-derived stem cells	• High yield • High proliferative rate • High chondrogenic potential	• Limited source of tissue

Embryonic Stem Cells

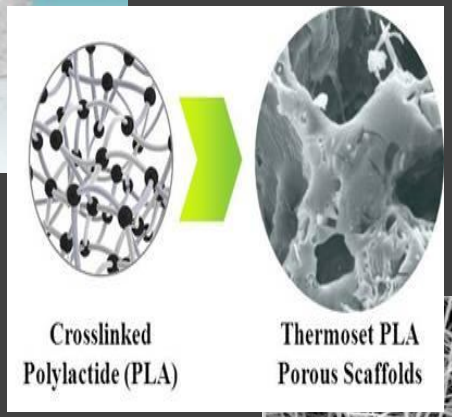
- Collected at the blastocyst stage (day 6) of embryogenesis
- Can differentiate into cells from all three germ layers of the body (endoderm, endoderm, mesoderm)
- Capable of self-renewal and undifferentiated proliferation in culture for extended time.

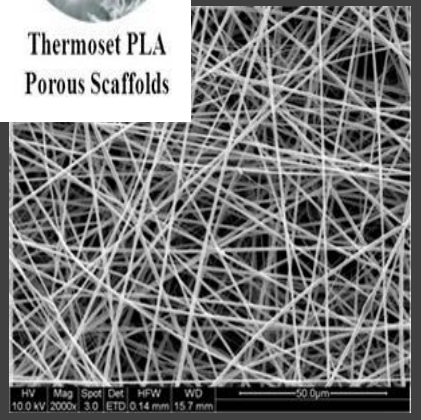
Chondrocytes and MSCs, Co-Culture Systems

Co-Culture	Advantages	Disadvantages
MSCs + Chondrocytes	• MSCs enhance proliferation of chondrocytes. • Chondrocytes inhibit the hypertrophy of the MSCs, by secreting hormones.	• Complexity. • Regulatory hurtles may hinder progress in cartilage repair applications.

Scaffolds

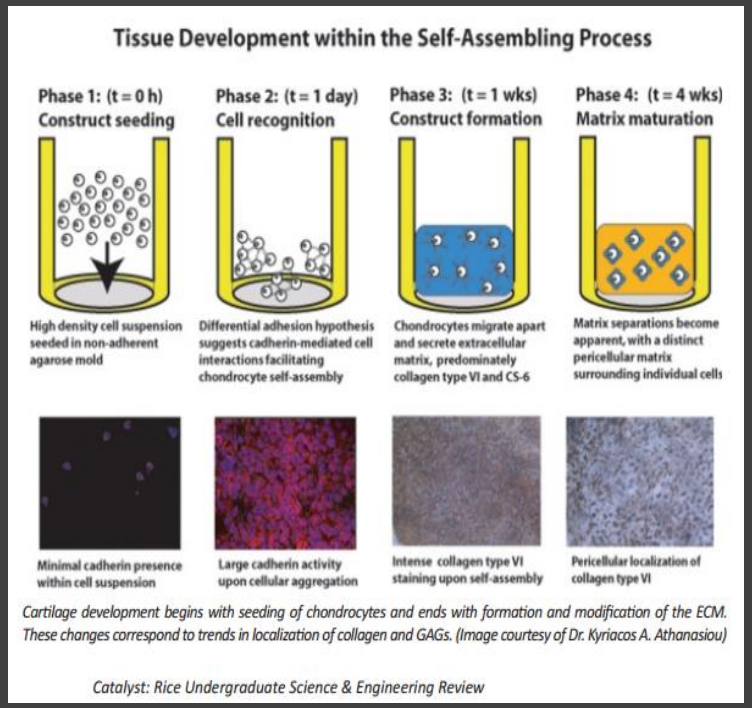
- Natural Scaffolds
  - Hyaluronic acid
  - Seaweed derived polysaccharides
  - Collagen(I,II)
- Synthetic Scaffolds
  - PLA
  - PGA
  - PLGA
- Nanostructured scaffolds
  - Nanofibrous





Scaffold-free Cartilage Tissue Constructs

- Scaffold free methods
  - Pellet Culture
  - Aggregate Cultures
  - Self assembling process
  - Advantages
    - Morphological change
    - No high cadherin and integrin activity
    - No gel encapsulation limit cell-cell communication



Biomolecules

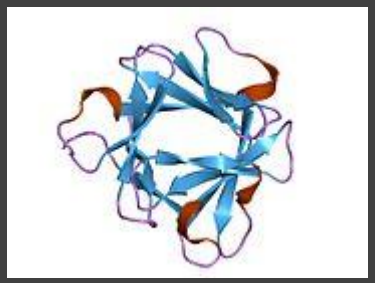
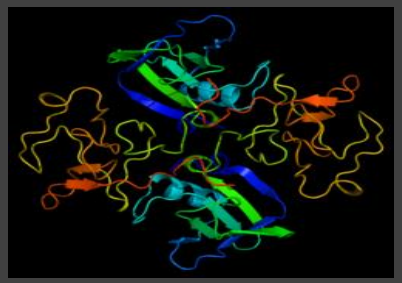
- Biomolecules are used to enhance stem-cell mediated chondrogenesis. Articular cartilage is inherently exposed to a range of biochemical and biophysical stimuli that affect its homeostasis and capacity for regeneration.

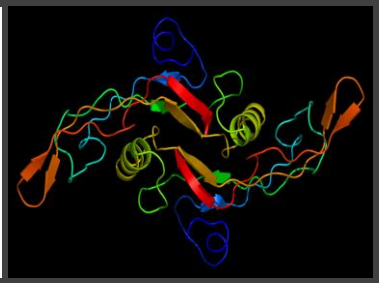
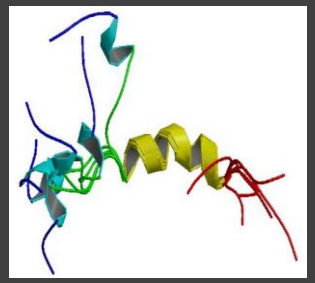
Biomolecules used:

- Cytokines.
- Hormones.
- Growth factors.

Growth Factors

- bFGF Basic Fibroblast Growth Factor
- HGF Hepatocyte Growth Factor
- PDGF Platelet-Derived Growth Factor
- TGF-β Transforming Growth Factor
- PTHrP Parathyroid Hormone Related Peptide

Mechanical Stimuli

- Dynamic shear of 1–25% at 0.01–3 Hz (0,1-24 Mpa) has been shown to increase ECM synthesis.
- Shear has also been shown to increase cartilage oligomeric matrix protein expression.
- Direct compression, as applied to tissue engineered constructs, has been mostly dynamic, as native cartilage has been shown to respond negatively to static loading.
- Rotating wall bioreactors have been shown to increase GAG content within engineered constructs beyond physiological levels, while maintaining collagen levels.

Conclusion

The latest research in the field of cartilage TE suggests a shift away from the use of chondrocytes to multipotent mesenchymal stem cells (MSCs). The identification of MSCs within different sources such as synovial and adipose tissue has offered a solution to the drawbacks associated with the use of chondrocytes.

The ever growing use of biomimetic approaches in designing biomaterials for cartilage defect repair demonstrates significant advances in this field.

Moreover, the incorporation of recombinant growth factors to further improve the chondro-inductivity and subsequent regenerative capacity of scaffolds may play a major role in development of constructs for large chondral defects.

Thank you.